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S	TAT	EMENT	BY APPLICANT	First Named Inventor	Stavros C. Manolagas, et al.		
				Group Art Unit	1614		
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Sheet	1	of	5	Attorney Docket No.	06572.105002		

			U.S. PA	TENT DOCUMENTS		
Examiner	Cite	U.S. Patent Docur	ment	Name of Patentee or Applicant of Cited	Date of Publication of	Pages, Columns, Lines, Where Relevant
Initials*	No.	Number	Kind Code (if known)	Document	Cited Document MM-DD-YYYY	Passages or Relevant Figures Appear
11/	AA	5,885,973		Papapoulos et al.	03-23-1999	
3	AB	5,859,001		Simpkins et al.	01-12-1999	
	AC	5,843,934		Simpkins, J.W.	12-01-1998	
	AD	5,824,672		Simpkins et al.	10-20-1998	
	AE	5,753,649		Tahara et al.	05-19-1998	
	AF	5,750,746		DeLuca et al.	05-12-1998	
	AG	5,674,844		Kuberasampath et al.	10-07-1997	
	AH	5,663,195		Scolnick	09-02-1997	
	Αl	5,618,549		Patat et al.	04-08-1997	
	AJ	5,604,259		Jee	02-18-1997	
	AK	5,593,988		Tahara et al.	01-14-1997	
	AL	5,593,833		Morrison et al.	01-14-1997	
	AM	5,565,444		Mizushima et al.	10-15-1996	
	AN	5,532,391		DeLuca et al.	07-02-1996	
	AO	5,532,226.		Demarest et al.	07-02-1996	
	AP	5,510,370		Hock	04-23-1996	
	AQ	5,414,098	1	DeLuca et al.	05-09-1995	
	AR	5,403,831		DeLuca et al.	04-04-1995	
	AS	5,354,773		Herslof et al.	10-11-1994	
T Y	AT	5,300,687		Schwender et al.	04-05-1994	

			F	OREIGN	PATENT DOCUMENTS			
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M	AU	PCT	WO 98/22113		Univ. of Florida Research Foundation	05-28-1998		
	AV	РСТ	WO 98/31381		Univ. of Florida Research Foundation	07-23-1998		
V	AW	PCT	WO 95/26719		Arcturus Pharmaceutical Corp.	10-12-1995		
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Examiner Initials*	Cite No.	Number	Kind Code (if known)	Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
K	CA	4,588,716		DeLuca et al.	05-13-1986	
7	СВ	4,522,811		Eppstein et al.	06-11-1985	
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Substitute for form 1449A/PTO		Complete if Known			
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			U.S. PA	TENT DOCUMENTS	· ·							
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Initials*							Number	Kind Code (if known)	Document	Cited Document MM-DD-YYYY	Passages or Relevant Figures Appear	
pr	FA	5,362,720	1	Labrie	11-08-1994	· · · · · · · · · · · · · · · · · · ·						
1	FB	5,189,212		Ruenitz	02-23-1993							
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				FOREIGN P	ATENT DOCUMENTS.		
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		OTHER PRIOR ART NON PATENT LITERATURE DOCUMENTS					
Examiner Initials*	I I Item (hook magazine jojirnal serial symnosium catalog etc.) date nage(s) volume-issue						
W	DA	BELLIDO, T. et al. Overexpression of Bcl-2 Renders Osteoblastic Cells Refractory to Glucocorticoid- Induced Apoptosis, Bone, 23:S324, 1998					
	DB	BELLIDO, T. et al. Regulation of Interleukin-6, Osteoclastogenesis, and Bone Mass by Androgens, J. Clin. Invest. 95:2886-2895 (1995)					
	DC	BERGGREN, M. et al. <u>Glutathione Biosynthesis in the Isolated Perfused Rat Lung: Utilization of Extracellular Glutathione</u> , Federation European Bicohemcal Societies, 176: 189-192 (1984)					
	DD	DEMPSTER, D.W., Exploiting and Bypassing the Bone Remodeling Cycle to Optimize the Treatment of Osteoporosis, Journal of Bone and Mineral Research. 12:1152-1154 (1997)					
	DE	DEMPSTER, D.W. New Concepts in Bone Remodeling In: Dynamics of Bone and Cartilage Metabolism (1999) Academic Press 261-273.					
	ELLIS, E. F. et al., Restoration of cerebrovascular responsiveness to hyperventilation by the oxyge pradical scavenger n-acetylcysteine following experimental traumatic brain injury, Journal of Neurosurgery. 75:774-779 (1991)						
	DG	ETTINGER, B. et al., Reduction of Vertebral Fracture Risk in Postmenopausal Women With Osteoporosis Treated with Raloxifene, Journal of the American Medical Association. 282:637-645 (1999)					
	DH	FITZPATRICK, L.A. <u>Selective Estrogen Receptor Modulators and Phytoestrogens: New Therapies for the Postmenaopausal Women</u> Mayo Clin. Proc. 74: 601-607 (1999)					
	DI	HUGHES, D.E. et al., Estrogen promotes apoptosis of murine osteoclasts mediated by TGF-, Nature Medicine. 2:10:1132-1136 (1996)					
	DJ	JILKA, R.L. et al., Osteoblast Programmed Cell Death (Apoptosis): Modulation by Growth Factors and Cytokines, Journal of Bone and Mineral Research. 13:793-802 (1998)					
	DK	JILKA, R.L. et al, Increased Osteoclast Development After Estrogen Loss: Mediation by Interleukin-6, Science 257:88-91 (1992)					
	DL	JILKA, R.L. et al., <u>Linkage of Decreased Bone Mass with Impaired Osteoblastogenesis in a Murine</u> <u>Model of Accelerated Senescence</u> , The Journal of Clinical Investigation. 97:1732-1740 (1996)					
	DM	JILKA, R.L. et al., Loss of Estrogen Upregulates Osteoblastogenesis in the Murine Bone Marrow, Evidence of Autonomy from Factors Released during Bone Resorption, The American Society for Clinical Investigation, Inc. 101:1942-1950 (1998)					
	DN	JILKA, R.L. et al., <u>Increased bone formation by prevention of osteoblast apoptosis with parathyroid hormone</u> , The Journal of Clinical Investigation. 104:439-446 (1999)					
	DO	KAMEDA, T. et al., Estrogen Inhibits Bone Resorption by Directly Inducing Apoptosis of the Bone- resorbing Osteoclasts, The Journal of Experimental Medicine. 186:489-495 (1997)					
Y	DP	KNIGHT, K.R. et al., <u>Enhancement of ischaemic rabbit skin flap survival with the antioxidant and free-radical scavenger N-acetylcysteine</u> , Clinical Science. 81:31-36 (1991)					
Examiner's Signature Date Considered							

Substitute for form 1449A/PTO Complete if Known Application Number 09/414,091 **INFORMATION DISCLOSURE** Filing Date October 7, 1999 **STATEMENT BY APPLICANT** First Named Inventor Stavros C. Manolagas, et al. Group Art Unit 1614 (use as many sheets as necessary) **Examiner Name** of 5 Attorney Docket No. Sheet 06572.105002

		OTHER PRIOR ART NON PATENT LITERATURE DOCUMENTS					
Examiner Initials*	Cite No. Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.						
M	ΕA	LALITHA, T. et al., Effect of N-Acetyl-cysteine, D-Penicillamine and Buthionine Sulfoximine on Glutathione Levels and CNS Oxygen Toxicity in Rats, Pharmacology & Toxicology. 66:56 -61 (1990)					
	EB	MANOLAGAS, S.C. et al., <u>Bone Marrow, Cytokines, and Bone Remodeling; Emerging Insights into the Pathophysiology of Osteoporosis</u> , New England Journal of Medicine. 332:305-311 (1995)					
	EC	NORRIS et al. Science 285:744-746 (1999)					
	ED	PAIGE, L.A. et al., Estrogen receptor (ER) modulators each induce distinct conformational changes in ER and ER, Proc. Natl. Acad. Sci. USA. 96:3999-4004 (1999)					
	EE	PARFITT, A.M., <u>Bone-Forming Cells in Clinical Conditions</u> In:Bone Vol. 1 The osteoblast and osteocyte. 351-430 (1996) CRC Press, Boca Raton					
	EF	PLOTKIN, L.I. et al., <u>Bisphosphonates Prevent Glucocorticoid-Induced Apoptosis of Osteocytes In</u> Vitro: a Putative Mechanism Influencing Mechanosensing, Bone. 23:S157 (1998)					
	EG	RAISZ, L.G., Estrogen and bone: New pieces to the puzzle, Nature Medicine. 2:1077-1078 (1996)					
	EH	SMILKSTEIN, M.J. et al., <u>Efficacy of Oral N-Acetylcysteine in the Treatment of Acetaminophen</u> <u>Overdose</u> , The New England Journal of Medicine. 319:1557-1562 (1988)					
		SNYDER, P.J. et al. Effect of Testosterone Treatment on Bone Mineral Density in Men Over 65 Years of Age J. Clin. Endocrin. Metab. 84: 1966-1972 (1999).					
		SUN, J. et al., Novel Ligands that Function as Selective Estrogens or Antiestrogens for Estrogen Receptor- or Estrogen Receptor-, Endocrinology. 140:800-804 (1999)					
	ΕK	WEINSTEIN, R.S. et al., <u>The Effects of Androgen Deficiency on Murine Bone Remodeling and Bone</u> <u>Mineral Density are Mediated via Cells of the Osteoblastic Lineage</u> , Endocrinology. 138:4013-4021 (1997)					
		WEINSTEIN, R.S. et al., <u>Inhibition of Osteoblastogenesis and Promotion of Apoptosis of Osteoblasts</u> and Osteocytes by Glucocorticoids, The Journal of Clinical Investigation. 102:274-282 (1998)					
	EM	WEINSTEIN, S. et al., <u>Anatomic Juxtaposition of Apoptotic Osteocytes and Avascular Necrosis in</u> Femurs from Patients with Glucocorticoid Excess, Bone. 23:S461 (1998)					
Ų	EN.	Catalogue from Steroids, Inc. PQ Box 310, Wilton, NH 03086 (undated)					
W		SPARKS, A.B. et al. <u>Screening phage-displayed peptide libraries</u> . In: Phage Display of Peptides and Proteins, A Laboratory Manual. 227-253 (1996) Academic Press, San Diego.	_				
Examiner's Signature		Date Considered 10/20/03					

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PTO/SB/08A (10-96)

Approved for use through 10/31/99. OMB 0651-0031

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INFORMATION DISCLOSURE	Filing Date	October 7, 1999		
STATEMENT BY APPLICANT	First Named Inventor	Stavros C. Manolagas, et al.		
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	U.S. PATENT DOCUMENTS									
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Examiner Initials*	Cite No.	Number	Kind Code (if known)		Publication of Cited Document MM-DD-YYYY	Where Relevant Passages or Relevant Figures Appear				
1/1	BA	5,260,290		DeLuca et al.	11-09-1993					
	ВВ	5,208,219		Ogawa et al.	05-04-1993					
	вс	5,183,815		Saari et al.	02-02-1993					
	BD	5,164,368		Recker	11-17-1992					
	BE	5,140,864		DeLuca et al.	04-14-1992					
	BF	5,118,667		Adams et al.	06-02-1992					
	BG	5,071,655		Baylink	12-10-1991					
	ВН	5,001,118		Maeda et al.	03-19-1991					
	ВІ	4,973,584		DeLuca et al.	11-27-1990					
	BJ	4,970,237		Jensen et al.	11-13-1990					
	ВК	4,870,063		Binderup et al.	09-26-1989					
	BL	4,870,054		Recker	09-26-1989					
	ВМ	4,833,125		Neer et al.	05-23-1989					
	BN	4,710,382		Recker	12-01-1987					
T T	ВО	4,619,920		DeLuca et al.	10-28-1986					

				FOREIGN P	ATENT DOCUMENTS		
		Foreign Patent Document					
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			U.S. PATENT DOCUMENTS		
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TK	AA	5,071,773	Evans et al.	12/10/1991	
	AB	5,298,429	Evans et al.	03/29/1994	
	AC	5,545,634	Labrie et al	08/13/1996	
	AD	5,506,102	McDonnell	04/09/1996	
	AE	5,554,601	Simpkins et al.	09/10/1996	
	AF	5,567,695	Labrie	10/22/1996	
	AG	5,846,960	Labrie ·	12/08/1998	
	AH	5,877,007	Housey	03/02/1999	
1	ΑI	6,080,779	Gasper et al.	06/27/2000	

			F	OREIGN PAT	TENT DOCUMENTS			
			Foreign Patent Do	cument			Pages, Columns,	
Examiner Initials *	Cite No. ¹	Office	³ Number Kind	Code ² (if known)	Date of Publication of Cited Document DD-MM-YYYY	Country	Lines, Where Relevant Passages or Relevant Figures Appear	T ⁶
pr	AJ	EP	0 753 523	Al	15/01/1997	EPO	-	
	AK	wo	00/19823	Al	13/04/2000	PCT		
	AL	wo	00/20007	A1	13/04/2000	PCT		
7	AM	WO	00/20625	A1	13/04/2000	PCT		
	AN	wo	00/37681	Al	29/06/2000	PCT		
V	AO	wo	99/54728	A3	28/10/1999	PCT		1

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U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

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		OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS	
Examiner Initials *	Cite No. 1	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ⁶
M	BA	ALESSI, D.R., et al. "PD 098059 Is a Specific Inhibitor of the Activation of Mitogen-activated Protein Kinase in Vitro and In Vivo," J. Biol. Chem. 270: 27489-27494 (1995).	
	BB	BELLIDO, T. et al. "Activation of the Janus Kinase/STAT (Signal Transducer and Activatior of Transcription) Signal Transduction Pathway by Interleukin-6-Tye Cytokines Promotes Osteoblast Differentiation," Endocrinology 138:3666-3676 (1997).	
	BC	FALKENSTEIN et al. "Nongenomically initiated steroid actions." Eur J Clin Invest. Dec 30 Suppl 3:51-4 (2000).	
	BD	FINKEL. "Phyto-oestrogens: the way to postmenopausal health." The Lancet. Nov 28;352(9142):1762.(1998).	
	BE	HILL et al. "Multiple extracellular signals promote osteoblast survival and apoptosis." Endocrinology 138(9): 3849-3858(1997).	•
	BF	KATO, Y. et al., "Establishment of an Osteocyte-like Cell Line, MLO-Y4," Journal of Bone and Mineral Research," 12:2014-2023 (1997).	
	BG	PARFITT. "Calcitriol for postmenopausal osteoporosis," Ann Intern Med. 1990 Jan 15;112(2):147	
V	ВН	XIA, Z. et al., "Opposing Effects of ERK and JNK-p38 MAP Kinases on Apoptosis," Science. 270:1326-1331 (1995).	

Examiner Signature # # C	Date Considered 23 po 103
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^{*}EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Unique citation designation number. ² See attached Kinds of U.S. Patent Documents. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶ Applicant is to place a check mark here if English language Translation is attached.